IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Juan C. Colberg et al.	**Examiner:**	Mark L. Berch
Serial No:	10/776,795	**Art Unit:**	1624
Filed:	February 16, 2004	**Docket:**	15905Z (PC10862B)
For:	COUPLING PROCESS AND INTERMEDIATES USEFUL FOR PREPARING CEPHALOSPORINS		

Confirmation No.: 4869
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22314-1450

DECLARATION UNDER 37 C.F.R. §1.132

Sir:

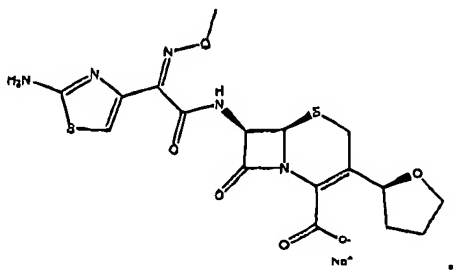
JUAN C. COLBERG, declares and says:

1. he received a PhD degree in Organic Chemistry from the University of Puerto Rico, Rio Piedras Campus, San Juan Puerto Rico, in 1994;

2. from 1993 to the present he has been and continues to be employed at Pfizer Inc., the assignee of the above-identified application;

3. he is a co-inventor in the above-identified patent application;

4. he was a member of a team which investigated the development of a commercial process for the synthesis of a long-acting cephalosporin having the generic name of cefovecin having the formula

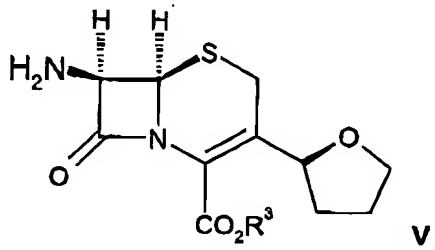


5. his group, in developing a commercial process for producing cefovecin, studied the process of Bateson, set forth in International Publication No. WO 92/01696;

6. the process set forth in Bateson was deemed inadequate for commercialization compared to the process his group developed as established by the claims of the above-identified application;

7. to substantiate the superiority of the process defined by the claims of the present application, the process disclosed by Bateson was compared to the claimed process of the above-identified application in experiments conducted by him or under his supervision;

8. utilizing the Bateson process, an ester compound having the formula V

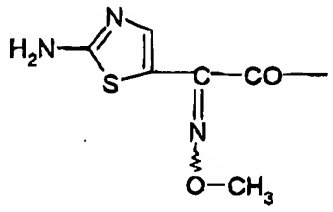


V

where R^3 represents 4-methoxybenzyl, was reacted, in a coupling reaction, with a compound having the formula III

$$R^2L \text{ (III)}$$

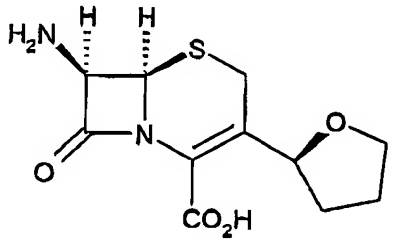
where L is chloride; and R^2 is



This coupling reaction step was followed by deprotection of the ester group, to produce cefovecin;

9. the form and purity of the product resulting from the reaction was unacceptable for further use due to an unacceptable high level of impurities. The crude product required purification by column chromatography and cefovecin was obtained in an overall yield of 30%. The yield was defined as the mass of cefovecin obtained as a percentage of the theoretical yield of cefovecin for the two step process;

10. the Bateson process was compared with the process of the present application wherein the a compound having the structural formula V, where R^3 is p-nitrobenzyl, was first deprotected to produce a compound having the structural formula II

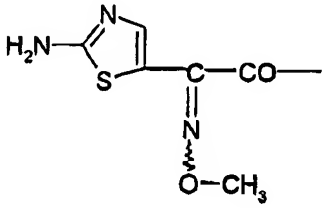


II

The compound II was thereupon reacted, in a coupling reaction, with a compound having the formula III

$$R^2L \text{ (III)}$$

where L is diethylphosphorothioate; and R^2 is



., to produce cefovecin;

;

11. the cefovecin product obtained by the practice of the claimed process of the present application was in a crystalline solid form of sufficiently high purity so that no purification operations were necessary prior to further use. Cefovecin product was obtained in a yield of

64%, where yield is again defined as the mass of cefovecin obtained as a percentage of the theoretical yield of cefovecin for the two step process;

12. the above results establish the clear superiority of the present process over the Bateson process. However, they are also very surprising in view of the well known sensitivity of Zwitterionic compounds, i.e. compounds containing both acidic and basic groups, of which compound II is one, to handling and changes in pH. That the compound having the formula II was produced and isolated in acceptable purity, as set forth in Example 2 of the specification of the present application, and that it was very useful in the synthesis of cefovecin was surprising; and

13. that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine, imprisonment, or both, under Section 1001 of Title 18 of the United States Code and such willful false statements may jeopardize the validity of the application or any patent issuing thereon;

Further declarant sayeth not.

Dated: December 16 2004

Juan C. Colberg